201-15635

DECHLORANE PLUS

CAS NO. 13560-89-9

HIGH PRODUCTION VOLUME (HPV) CHEMICAL CHALLENGE PROGRAM

TEST PLAN

Prepared for:

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EXECUTIVE SUMMARY

Occidental Chemical Company voluntarily submits for review and public comment the test plan for the chemical, Dechlorane Plus (1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a, 11,12,12a-dodecahydro-1,4:7,10-dimethanodibenzo[a,e]cyclooctene; CAS No. 13560-89-9), for review under the Environmental Protection Agency's High Production Volume (HPV) Chemicals Challenge Program. Available data and Endpoint data gaps are summarized in Table 1.

Table 1. Data Assessment Matrix

Endpoint	Number of Studies Available	Best Reliability	Data Gap
Physico-Chemical Properties			
Melting Point	1	2	N
Density	2	2	N
Vapor Pressure	1	2	N
Partition Coefficient	1	2	N
Water Solubility	2	2	N
Solubility in various organic solvents	1	2	N
Volatility	1	2	N
pH	1	2	N
Environmental Fate			
Photodegradation	1	2	N
Stability in Water	1	3	Y
Transport between Environmental Compartments (water - soil adsorption)	1	2	N
Biodegradation			
Aerobic	3	2	N
Anaerobic	1	3	Y
Bioaccumulation	4	2	N
Ecotoxicity			
Acute Toxicity to Fish	2	3	N
Acute Toxicity to Aquatic Invertebrates	N		Y
Toxicity to Aquatic Plants	N		Y
Mammalian Toxicity			
Acute Toxicity	7	2	N
Repeated Dose Toxicity	3	2	N
Genetic Toxicity *in Vitro*	4	2	N
Genetic Toxicity *in Vivo* / *in Vitro*	N		Y
Toxicity to Reproduction	N		Y
Developmental Toxicity	N		Y

CONTENTS

I. INTRODUCTION

Occidental Chemical Company (OxyChem) has committed voluntarily to develop screening level physicochemical properties, environmental effects and fate, and human health effects data for Dechlorane Plus, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro-1,4:7,10-dimethanodibenzo[a,e]cyclooctene under the Environmental Protection Agency's (EPA's) High Production Volume (HPV) Challenge Program ("Program").

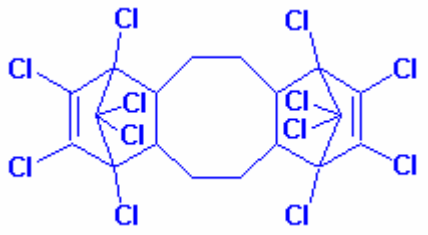
This plan identifies the chemical, its CAS number, existing data of adequate quality, and outlines testing planned to develop screening level data for the chemical under the Program. The objective of this effort is to identify and develop sufficient test data and/or other information to adequately characterize the environmental fate and human health effects for the chemical in compliance with the EPA HPV Program.

II. DESCRIPTION OF THE HPV CHEMICAL

A. STRUCTURE AND NOMENCLATURE

The following is a structural characterization of Dechlorane Plus and associated nomenclature.

- 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro-1,4:7,10-dimethanodibenzo[a,e]cyclooctene
- Empirical formula: $C_{18}H_{12}Cl_{12}$
- CAS No. 13560-89-9
- Structural formula:



- Synonyms:

  Dodecachlorododecahydrodimethanodibenzocyclooctene
  Dechlorane Plus
  Dechlorane Plus 25
  Dechlorane Plus 35
  Dechlorane Plus 515

III. TEST PLAN RATIONALE AND ADEQUACY OF DATA

The information obtained and included to support this Test Plan has come from either internal studies conducted by/or for OxyChem (or its predecessor, Hooker Chemical Corporation), peer-reviewed scientific literature, or predictive environmental models. This initial assessment includes information on physicochemical properties, environmental fate, and possible human health effects associated with Dechlorane Plus. The data used to support this Test Plan include those Endpoints identified by the EPA (1998). Studies have been identified for each data Endpoint and summarized in the Screening Information Data Set (SIDS), which is located in Appendix 1. Additional information has been identified and included in the SIDS, although this information does not fulfill any Endpoint data gaps. This information is relevant to the Test Plan and is discussed in Section V.

All studies were reviewed and assessed for reliability according to standards specified by Klimisch *et al*. (1997), as recommended by the EPA (1999). Those studies receiving a rating of 1 or 2 are considered adequate by themselves to support data assessment needs. A study receiving a rating of 3 is considered inadequate by itself to support data assessment needs. However, some different studies rated 3 may corroborate a specific conclusion and together these studies are considered to fulfill a particular data assessment need.

IV. RELEVANT AVAILABLE INFORMATION

All available studies were reviewed, assessed for adequacy, and included in the SIDS document in Appendix 1. Those fulfilling specific Endpoints are described briefly in this section. Additional information, which does not fulfill Endpoints, is included in a discussion of the Test Plan (Section V).

A. PHYSICOCHEMICAL PROPERTIES

Dechlorane Plus is a white, crystalline, odorless, powder, with a molecular weight of 654 daltons. All major physicochemical parameters (See Table 2) relevant to environmental fate and human health effects received a reliability rating of 2.

Table 2. Physicochemical Parameters

Property	Value
Melting Point	350 deg C with decomposition
Density	1.8 g/cc
Vapor Pressure	0.006 mm Hg @200 deg C
Partition Coefficient (log Pow)	9.3
Water Solubility	44 ng/L - 249 ug/L (insoluble)
pH (methanol-water extract)	6.0 – 8.0
Volatility (4 hours at 100 deg C at 5 mm Hg)	0.12% maximum

Conclusion - No additional testing is recommended.

B. ENVIRONMENTAL FATE

These data are summarized in Table 3 below and the studies are briefly reviewed beginning on the next page.

Table 3. Environmental Fate Parameters

Endpoint	Value
Photodegradation	>24 years
Stability in Water	Stable (qualitative)
Transport between Environmental Compartments (water - soil sorption partition coefficient)	4.5×10^6
Biodegradation	Minimal or no aerobic degradation
Bioaccumulation	Yes in fish

1. Photodegradation

Photodegradation in water was determined in a study utilizing a light source that provided several lines of high photon fluxes in the solar spectral region above 290 nm. Dechlorane Plus was tested in the study for 168 hours, after which the photolysis half-life was calculated from the analytical results. The photolytic half-life in water was estimated to be >24 years.

2. Stability in Water

Based on first-order rate constants for cyclohexanes, which are structurally similar to Dechlorane Plus, the investigators decided it was unnecessary to quantitatively determine the half-life of Dechlorane Plus. Peroxyl radical oxidation of Dechlorane Plus was determined not to be an important transformation process.

3. Transport between Environmental Compartments (Water - Soil Adsorption)

Lake sediment was used in a 6-week study to determine the extent of partitioning of Dechlorane Plus from water into soil. The calculated sorption partition coefficient (Kp) was 4.5×10^6 (+/- 1.9×10^6). Dechlorane Plus preferentially adsorbed to the sediment.

4. Biodegradation

In three aerobic and one anaerobic biodegradation studies, Dechlorane Plus was tested for degradation in mineralized distilled water or BOD dilution water incubated with appropriate sewage sludge organisms for up to 6 weeks. Either Dechlorane Plus was not biodegradable or minimally biodegradable (with CO2 as a possible metabolite), or its extremely low water solubility prevented the bacteria in the domestic sewage from contacting and degrading the test substance.

5. Bioaccumulation

In four subchronic bioaccumulation studies, fish were dosed with Dechlorane Plus for up to 30 days, with the test substance either suspended in water or mixed in food. In these studies, any toxicity observed was not considered treatment related but rather a result of the use of a solvent because Dechlorane Plus is practically insoluble in water.

In one study, equilibrium of tissue accumulation was reached after 7 days of exposure with accumulated concentration in tissues of up to 8.8 ppm. Because of limited water solubility, BCFs were estimated from the octanol-water partition coefficient, water solubility, and the sediment-water partition coefficient, instead of study data. The BCFs were in poor agreement: 7.02 at 48 hours and 1.97 at 96 hours. Dechlorane Plus was found to bioaccumulate in fish after subacute or subchronic administration.

Conclusion - Stability in water and anaerobic biodegradation are recommended for testing to fulfill HPV data requirements. For other Endpoints, testing is not recommended.

C. ECOTOXICOLOGY

1. Acute Toxicity to Fish

Dechlorane Plus was tested for toxicity to freshwater fish in two studies, one static and one flow through for a period of 4 days. Because of the low water solubility, Dechlorane Plus remained suspended as particulates, sank to the bottom of the test vessels, or floated on the surface. There was no mortality or other adverse effects observed during either test. For both studies, the median tolerance limit (TL50) was >100 ppm, the highest concentration tested.

Conclusion - Toxicity to aquatic invertebrates and plants are recommended for testing to fulfill HPV data requirements. For other Endpoints, testing is not recommended.

D. HUMAN HEALTH

These data are summarized in Table 4 below and the studies are briefly reviewed beginning on the next page.

Table 4. Mammalian and Genetic Toxicity

Endpoint	Value
Acute Toxicity	
Oral (LD50)	>25,000 mg/kg bw
Inhalation (LC50)	> 300 mg/l
Dermal (LD50)	>8000 mg/kg bw
Dermal Irritation	Not or mild irritant
Eye Irritation	Not an irritant
Sensitization	Not a sensitizer
Repeated Dose Toxicity	
Inhalation (LOAEL)	0.640 mg/L
Oral feed (NOAEL)	100,000 ppm
Dermal (NOAEL)	2000 mg/kg bw/day
Genetic Toxicity *in Vitro*	
Ames	Negative
Mouse Lymphoma	Negative

1. Acute Toxicity

For the two acute oral toxicity studies, the two inhalation studies, and the one dermal toxicity study, the Median Lethal Dose or Concentration (LD50 or LC50) was greater than the highest dose tested for each study. No adverse effects were observed for any animal in any of the studies.

One eye irritation study and one dermal sensitization study were performed with Dechlorane Plus. The test substance was not an eye irritant and was not a sensitizer. No dermal irritation studies were available, but after repeated dermal exposures in rabbits and guinea pigs, at most mild irritation was observed.

2. Repeated Dose Toxicity

Three subchronic toxicity studies were performed with Dechlorane Plus, one 28-day dermal, one 28-day inhalation, and one 90-day oral dietary study. In the 28-day dermal toxicity study, treated female rabbits had statistically-significant dose-related decreases in absolute and relative liver and ovary weights. There were no corresponding histopathological effects observed. The systemic NOAEL was 2000 mg/kg bw/day, the highest dose tested.

In the 28-day inhalation study, treated male and female rats had significantly increased absolute liver weights and low-dose females and high-dose males and females had significantly increased absolute lung weights. Associated treatment-related histopathological lesions consisted of increased numbers of macrophages in the alveoli and hepatocytomegaly of centrilobular hepatocytes in all treated male rats and in 2 of 5 high-dose females. There was no NOAEL for this study; the LOAEL was 0.640 mg/L. In the 90-day dietary toxicity study there were no statistically-significant adverse effects observed in any parameters examined. The NOAEL was 100,000 ppm, the highest dose tested.

3. Genetic Toxicity '*In Vitro*'

In two bacterial reverse mutation assays, Dechlorane Plus or the urine from rats administered Dechlorane Plus was tested for mutagenicity utilizing *Salmonella typhimurium* strains with and without metabolic activation. No toxicity or dose-related increases in the number of histidine revertants over background was observed in any of the three tests.

In one mouse lymphoma L5178Y TK+/- assay, Dechlorane Plus was tested for mutagenicity in mammalian cell cultures with and without metabolic activation. Dechlorane Plus was not cytotoxic and did not significantly increase the mutation frequencies above the spontaneous control frequency.

Conclusion – A tiered approach is recommended to determine the extent of testing to fulfill HPV data requirements. Relevant *in vitro* or *in vivo* genetic toxicity studies for chromosomal aberrations are recommended for testing. The results when reviewed with the data from repeated dose toxicity studies and from an available toxicokinetic study (See SIDS in Appendix 1) would then determine whether reproductive/developmental testing is necessary.

E. DATA EVALUATION

Adequate studies with Dechlorane Plus have been conducted for the endpoints listed in Table 5 below. These studies are considered adequate to support data assessment needs, either because at least one of the studies for that Endpoint has received a reliability score of 2 or because the results from studies for that Endpoint, even if inadequate, are corroborated by the results from other studies. For example, the two acute fish toxicity studies are inadequate by themselves to fulfill that Endpoint; however, there were three bioaccumulation studies, which lasted up to 30 days with the same species of fish and which resulted in no mortality to those fish. Consequently, the Acute Toxicity to Fish Endpoint is considered fulfilled by the corroborative data.

Table 5. Studies Fulfilling Endpoints

Physico-Chemical Properties
Environmental Fate
Photodegradation
Transport between Environmental Compartments (water - soil adsorption)
Biodegradation, aerobic
Bioaccumulation
Ecotoxicity
Acute Toxicity to Fish
Mammalian Toxicity
Acute Toxicity
Repeated Dose Toxicity
Genetic Toxicity *in Vitro*

V. TEST PLAN SUMMARY

A tiered approach is recommended to determine the extent of testing to fulfill HPV data requirements. This tiered approach prioritizes the data gaps based on related relevant data and the potential hazards from exposure. The following studies are recommended:

Tier 1:

- Conduct relevant *in vitro* or *in vivo* genetic toxicity studies. The results when reviewed with the data from repeated dose toxicity studies and from an available toxicokinetic study (See SIDS in Appendix 1) would then determine whether reproductive/developmental testing is necessary.
- Conduct the following ecotoxicity studies: Acute Toxicity to Aquatic Invertebrates and Toxicity to Aquatic Plants. Because Dechlorane Plus appears to have ecotoxicological effects in fish and it appears to selectively adsorb to soil from water, organisms that associate with the sediment of waterways may be adversely affected by Dechlorane Plus.

Tier 2:

- Conduct a reproductive/developmental screening study. In the 28-day dermal study in rabbits, there were significant, dose-related decreases in absolute and relative ovary weights but there were no corresponding histopathological effects observed. In a toxicokinetics study performed with Dechlorane Plus in rats, ovaries and liver had the greatest concentrations of Dechlorane Plus (See SIDS in Appendix 1).

Tier 3:

Environmental fate data are extensive and indicate that Dechlorane Plus is minimally water soluble and likely will not biodegrade. Conducting the following studies would fulfill data gaps but they are unlikely to result in any additional information. Thus, these two studies are not recommended for immediate testing.

- Conduct a Water Stability study. Considering that Dechlorane Plus appears to have ecological effects on fish (and possibly on other aquatic organisms), this property should be better defined.
- Conduct an Anaerobic Biodegradation study. Although the aerobic biodegradation study results indicate that Dechlorane Plus does not biodegrade, the anaerobic study methodology and conditions do not allow us to conclude that Dechlorane Plus behaves comparably under anaerobic conditions.

Summaries of results will be produced when data and analyses are available. This test plan is expected to provide adequate data to characterize the human health effects and environmental fate and effects endpoints under the Program. OxyChem does not believe additional information is needed to fulfill Endpoint data gaps other than those described in the paragraphs above.

VI. REFERENCES

Klimisch, H.-J., Andreae, M. and U. Tillman. 1997. A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regul. Toxicol. Pharmacol*. 25:1-5.

United States Environmental Protection Agency (EPA). 1998. Guidance for meeting the SIDS requirements (The SIDS Guide). Guidance for the HPV Challenge Program (11/31/98).

United States Environmental Protection Agency (EPA). 1999. Determining the adequacy of existing data. Guidance for the HPV Challenge Program (2/10/99).